510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k111128

B. Purpose for Submission:

New Device

C. Measurand:

Glycosylated hemoglobin (HbA1c)

D. Type of Test:

Quantitative

E. Applicant:

Ceragem Medisys Inc.

F. Proprietary and Established Names:

LabonaCheck A1c

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LCP	Class II	21 CFR 864.7470	Hematology, 81

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

The LabonaCheck™ A1c is intended for the quantitative measurement of glycated hemoglobin in venous whole blood and capillary fingerstick samples. This device is intended for multiple patient, professional use. Measurement of percent glycated hemoglobin (HbA1c) is effective in monitoring long-term glucose control in individuals with diabetes mellitus by using the LabonaCheck™ A1c. Only auto-disabling, single use lancing devices should be used with this system.

3. Special conditions for use statement(s):

   - Clinical Settings and Point-of-Care
   - Not for screening or diagnosis of diabetes
   - Should not be used to test patients with hemoglobinopathies of HgbF

4. Special instrument requirements:

   LabonaCheck™ A1c analyzer.

I. Device Description:

The LabonaCheck™ A1c HbA1c test kit contains reagents, cartridge membrane filters and a washing solution. Each box of test kits contains 24 cartridge membrane filters, which is sufficient for 24 tests. The reagents are comprised of an R1 and an R2 reagent which are ready to use. The R1 reagent contains: 0.2mg/ml boronate derivative, 6.2% organic solvent, and 0.15% lysing agent. The R2 reagent contains: 0.5% detergent. The cartridge membrane filter consists of A/B and GA100 Glass fiber and Nylon.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   NycoCard® HbA1c Glycated Hemoglobin Assay

2. Predicate 510(k) number(s):
   k993131

3. Comparison with predicate:

Similarities		
Item	Device LabonaCheck™ A1c	Predicate NycoCard® HbA1c Glycated Hemoglobin Assay k993131
Intended Use	For the quantitative determination of percent glycated hemoglobin in	Same

Similarities		
Item	Device LabonaCheck™ A1c	Predicate NycoCard® HbA1c Glycated Hemoglobin Assay k993131
	venous whole blood and capillary fingerstick samples.	
Detection Method	Boronate affinity	Same
Sample Volume	5 µl	Same
Test Time	3 minutes	Same
Measuring Range	4-15% HbA1c	Same

Differences		
Item	Device LabonaCheck™ A1c	Predicate NycoCard® HbA1c Glycated Hemoglobin Assay k993131
Battery	CR2032	NiMH

K. Standard/Guidance Document Referenced (if applicable):

EN ISO 14971 Medical Devices-Application of Risk Management Devices

CLSI EP5-A: Evaluation of precision performance of clinical chemistry devices

CLSI EP6-A: Evaluation of Linearity of quantitative measurement procedures

CLSI EP7-A: Interference testing clinical chemistry

CLSI EP9-A2: Method Comparison and bias estimation using patient samples

CLSI EP15-P: User Demonstration of Performance for precision and accuracy

L. Test Principle:

The LabonaCheck A1c is a boronate affinity assay. When blood is added to the R1 reagent, the erythrocytes immediately lyse and all hemoglobin is precipitated. The boronic acid conjugate binds to the cis-diol configuration of glycated hemoglobin. An aliquot of the reaction mixture is added to the cartridge and all the precipitated hemoglobin, conjugate-bound and unbound, remains on top of the filter. Any unbound boronate is removed with the

washing solution. The precipitate is evaluated by measuring the blue (glycated hemoglobin) and the red (total hemoglobin) color intensity respectively with LabonaCheck A1c HbA1c analyzer, the ratio between them being proportional to the percentage of HbA1c in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

An internal precision study was conducted using venous blood samples at 5 different HbA1c concentrations over the measuring range of the device. Samples were analyzed twice/day for 20 days using 2 analyzers and two lots of test cartridges (n=80). Results were as follows:

Total Precision:

Sample #	**%HbA1c (mean)**	**N**	**Within Run**		**Day to Day**		**Total**	
			SD	CV(%)	SD	CV(%)	SD	CV(%)
1	4.3	80	0.1	3.0	0.1	2.8	0.1	3.0
2	6.2	80	0.1	2.2	0.1	2.0	0.2	2.6
3	8.9	80	0.2	2.2	0.1	1.5	0.2	1.9
4	11.7	80	0.2	2.1	0.2	1.3	0.3	2.2
5	14.3	80	0.2	1.6	0.2	1.7	0.2	1.6

An external precision study was conducted at 3 point-of-care sites with 2 operators per site. Two kit lots and three LabonaCheck HbA1c analyzers were used. Each operator analyzed 3 venous whole blood samples with values ranging from 4.0-14.0% HbA1c. Results were as follows:

Precision (Per Site):

Sample #	**POC Site 1**			**POC Site 2**			**POC Site 3**		
	Mean(%)	SD	CV(%)	Mean(%)	SD	CV(%)	Mean(%)	SD	CV(%)
1	4.8	0.15	3.0	4.9	0.17	3.4	4.9	0.16	3.2
2	8.8	0.28	3.2	8.9	0.29	3.2	8.7	0.28	3.2
3	13.2	0.4	3.3	13.2	0.4	3.1	13.3	0.5	3.5

Sample #	**3 sites combined**		
	Mean(%)	SD	CV(%)
1	4.9	0.16	3.2
2	8.8	0.28	3.2
3	13.2	0.4	3.3

b. Linearity/assay reportable range:

Two samples with values of 3.2% and 17.5% HbA1c were mixed in varying proportions to make 7 test samples spanning the measuring range of the device. Testing was performed using two lots of test kits. HbA1c recoveries of the observed versus the expected concentrations were 100-108% across the measuring range. Linear regression is:

$$y=0.968x+0.238,\ r^2=0.999$$

The claimed measuring range for the LabonaCheck™ A1c is 4.0 – 15% HbA1c.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Controls- External control materials are purchased separately. Control materials were previously cleared under k043070.

The labeling states that venous whole blood samples can be stored up to 7 days at 2-8˚C

Traceability-The LabonaCheck™ A1c is certified with the National Glycohemoglobin Standardization Program (NGSP). The NGSP certification expires in one year. See NGSP website for current certification at http://www.ngsp.org.

d. Detection limit:

The limit of Blank (LoB) and Limit of Detection (LoD) were determined by assaying a zero sample (blank) and five low HbA1c samples according to CLSI guideline EP17-A. Each sample was assayed twice a day in replicates of ten (n=60) for three days on LabonaCheck™ A1c.

LoB= 3.1%, LoD=3.3%

The claimed measuring range, 4% -15% HbA1c, is based on linearity. See 1b. above

e. Analytical specificity:

Studies were performed to assess common or known substances that could interfere with the assay. Whole blood samples with A1c% concentrations of 4.5%, 8.5%, and 11.1% were evaluated in duplicate at a low and high level for each interferent. Observed A1c% values were compared to the control samples whose A1c% was determined by a NGSP certified method. The sponsor's acceptance criterion is ≤10% bias between the test and the control samples. Results are summarized below:

Interferant	Concentration showing no interference
Ascorbic Acid	6 mg/dL
Bilirubin (Conjugated)	5 mg/dL
Bilirubin(Unconjugated)	15 mg/dL
Glucose	1200 mg/dL
Hemoglobin	20 g/dL
Lipid (Triglyceride)	500 mg/dL
Albumin	5 g/dL
K3 EDTA	300 mg/dL
Heparin	8000 U/dL
Sodium fluoride	1000 mg/dL
Sodium citrate	3.20%
Acetaminophen	30 mg/dL
Metformin	4 mg/dL
Acetylsalicylic acid	1000 mg/dL
Glybenclamide	5 mg/dL
Ibuprofen	40 mg/dL
Rheumatoid Factor	300 IU/mL

Hemoglobin Variant Interference

Cross-reactivity to hemoglobin variants was examined using patient samples containing known concentrations of HbA1c and each variant. The variants and the ranges in which they were tested are as follows: HbA0, HbA1a, HbA1b, HbF, HbC, HbD, HbE and HbS. Each sample was tested in duplicate, and the difference between the known concentration of the reference analyzer (Trinity (Primus) Boronate Affinity HPLC) and the values obtained with the LabonaCheck™ A1c device were calculated.

No significant bias of greater than ±10% was observed in the presence of HbA0, HbA1a, Hba1b, HbC, HbD, HbE or HbS.

The labeling states "Fetal Hemoglobin (HbF) consists of two alpha and two gamma chains that are not recognized by the anti-HbA1c antibody. Samples that contain high amounts of HbF (>22.7%), usually found in some people with thalassemia, in infants, and in some pregnant women, may yield a lower than expected HbA1c result with this assay."

Carbamylated Hemoglobin Interference

An interference study was performed to assess the affect of carbamylated A1c with the LabonaCheck™A1c assay. Whole blood pools were prepared to create a low (~4.7 – 5.4% HbA1c), a medium (~7.2 – 8.0 % HbA1c) and a high (~10.6 – 10.9 %

HbA1c) sample. Sodium cyanate was spiked into the samples at a low concentration (2.5mmol/L) and a high concentration (5mmol/L). The samples were incubated for two hours at 37˚C. The low, medium and high samples were tested in duplicate on the LabonaCheck™ analyzer and compared to the control sample. The sponsor's acceptance criterion is ≤10% bias between the test and control samples.

The sponsor concluded that carbamylated A1c does not interefere with the LabonaCheck™A1c device.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was conducted at two hospital laboratories using a total of 50 fresh whole blood EDTA samples. The EDTA venous blood samples were analyzed with the LabonaCheck™A1c, NycoCard®HbA1c (predicate device), and Tosoh HLC-723 GHB G7 (reference method). Samples were analyzed in singlicate on the reference method and in duplicate on the candidate and predicate devices. Sample range tested was 4.2 – 14.5 HbA1c%. The linear regression correlation using only the first set of replicates measured on the LabonaCheck™A1c as compared to the Tosoh HLC-723 GHB G7 is as follows:

	Slope	Intercept	r
LabonaCheck vs Tosoh	0.9783	-0.0652	0.9933
LabonaCheck vs.NycoCard	1.0321	-0.1075	0.9921

A method comparison study was performed at three Point-of-Care sites. 40 fresh venous EDTA samples with an HbA1c% ranging from 4.5-14.0% were analyzed at each site with two LabonaCheck™A1c analyzers and one Tosoh HLC-723 GHB G7 (internal lab device). All samples were analyzed in duplicate. The linear regression correlation using only the first set of replicates is as follows:

	n	Slope	Intercept	r
Site 1	40	1.0225	-0.2129	0.9877
Site 2	40	0.9868	0.0516	0.9848
Site 3	40	0.9915	0.0756	0.9886
Combination of all 3 sites	120	1.000	-0.0292	0.9970

An additional method comparison study was performed at three Point-of-Care sites. 40 capillary whole blood fingerstick samples with an HbA1c% ranging from 4.2-14.8% were analyzed at each site with two LabonaCheck™A1c analyzers and on one Tosoh HLC-723 GHB G7 (internal lab device). All samples were analyzed in duplicate. The linear regression correlation using only the first set of replicates is as follows:

	n	Slope	Intercept	r
Site 1	40	1.0014	0.1793	0.9864
Site 2	40	0.9525	0.5416	0.9840
Site 3	40	0.9698	0.4475	0.9878
Combination of all 3 sites	120	0.9744	0.3903	0.9858

b. Matrix comparison:

A matrix comparison study was performed using K_3EDTA, Sodium Heparin, and NaF tubes. K_3EDTAwas used as the reference anticoagulant. 40 samples were analyzed for HbA1c. Each single set of samples was analyzed on the LabonaCheck ™ A1c analyzer and values obtained versus the Tosoh G7 (reference analyzer). Samples ranged from 4.5 - 14.1%) The linear regression analyses are as follows:

K_3EDTA vs. Sodium Heparin – $y=0.9682x + 0.319$, $R^2=0.967$

K_3EDTA vs. Na Fluoride – $y=0.9487x + 0.4364$, $R^2=0.9569$

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Reference Range[1]

	NGSP	IFCC
Increased risk for diabetes	≥6.5%	≥48mmol/mol

[1]American Diabetes Association Clinical Practice Recommendation, January 2010;33 (supplement 1).

N. Instrument Name:

LabonaCheck™ A1c analyzer

O. System Descriptions:

1. Modes of Operation:

   The test cartridge and pre-filled test tube containing R1/Reagent are for single use only and must be replaced when performing a new test. The R2/Reagent (diluent) is for use with multiple cartridges.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X___ or No _____

3. Specimen Identification:

   There is no sample identification function with this device. Samples are applied directly to the test cartridge as they are collected.

4. Specimen Sampling and Handling:

   Fingerstick capillary whole blood, or 5µl venous whole blood with or without anticoagulants (K_3EDTA, heparin and NaF) are added to the pre-filled test tube containing R1/Reagent. 25µl of the sample, mixed with the R1 reagent, is then applied to the test cartridge. 25 µl of R2/Reagent (diluent) is then added to the test cartridge containing the sample. Test cartridge is then placed into the analyzer tray for analysis.

5. Calibration:

   The LabonaCheck™ uses a calibration plate which is factory calibrated and is not adjustable. An initial calibration is performed when the analyzer is powered on and additional calibrations are automatically performed every 24 samples.

6. Quality Control:

   Quality Control is analyzed in the same manner as patient samples. Labeling recommends that a normal and abnormal control be assayed daily according to state, federal and local guidelines and 1) when using a new shipment of reagents 2) when using a new lot of reagent 3) whenever test results are in doubt 4) when training new operators 5) when the analyzer is strongly impacted by external influences 6) after maintenance or service.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

None

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.